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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
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(54) Title: IMMUNIZATION WITH PORPHYROMONAS GINGIVALIS PROTECTS AGAINST HEART DISEASE

(57) Abstract: The invention is directed to a method of preventing and treating a patient having a risk factor and/or a symptom of cardiovascular disease using an immunogenic composition comprising an immunogenically effective portion of Porphyromonas gingivalis in a pharmaceutically effective carrier substance, and a vaccine for same.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

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B. FIELDS SEARCHED

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
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Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MEDLINE, PUBMED

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Database EMBASE on STN, AN:1999208848, DESHPANDE, R.G. ET AL, Invasion strategies of the Oral Pathogen Porphyromonas gingivalis: Implication for Carovascular Disease, Invasion and Metastasis, 1998, Vol.18, No. 2, pages 57-69. See the Abstract.	1-7
Y	Database MEDLINE on STN, AN:1998389923, HERZBERG, M C. ET AL, Dental Plaque, Platelets and Carovascular Diseases, Annals of Periodontology, The American Academy of Periodontology, July 1988, Vol. 3, No. 1, pages 151-160. See the Abstract.	1-7
Y	Database EMBASE on STN, AN:1998417201, LAMONT, R.J. ET AL, Life Below the Gum Line: Pathogenic Mechanisms of Porphyromonas gingivalis, Microbiology and Molecular Biology Reviews, 1998, Vol. 62, No. 4, pages 1244-1263. See the Abstract.	1-7
Y	Database EMBASE on STN, AN:2001371735, LOESCHE, W.J. ET AL, Peridontal Disease as a Specific, Albeit Chronic, Infection: Diagnosis and Treatment, Clinical Microbiology Reviews, 2001, Vol. 14, No. 4, pages 727-752. See the Abstract.	1-7



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INTERNATIONAL SEARCH REPORT

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C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Database BIOSIS on STN, AN:2002:176618, CHEN, Z. ET AL, Protease-active Extracellular Protein Preparations for Porphyromonas gingivalis, Abstracts of the General Meeting of the American Society for Microbiology, 2001, Vol. 101, pages. 117-118. See the Abstract.	1-7
Y	Database CABI on STN, AN:2000:145383, WHITAKER ET AL, Effect of an Essential Oil-containing Antiseptic Mouthrinse on Induction of Platelet Aggregation by Oral Bacteria In Vitro, Journal of Clinical Periodontology, 2000, Vol. 27, No.5, pages 370-373. See the Abstract.	1-7
X	SHAPIRA ET AL, The Effects of Stress on the Inflammatory Response to Porphyromonas gingivalis in a Mouse Subcutaneous Chamber Model, Journal of Periodontology, March 1999, Vol. 70, No. 3, pages 289-292. See the entire document.	8-12
X	VASEL ET AL, Shared Antigen of Porphyromonas gingivalis and Bacteroides forsythus, Oral Microbiology and Immunology, 1996, Vol. 11, No. 4, pages 226-235. See the entire document.	8-12
X	GENCO ET AL, A Peptide Domain on Gingipain R Which Confers Immunity Against Porphyromonas gingivalis Infection in Mice, Infection and Immunity, September 1998, Vol. 66, No. 9, pages 4108-4114. See the entire document.	8-12
X	GENCO ET AL., Influence of Immunization of Porphyromonas gingivalis Colonization and Invasion in the Mouse Chamber Model, Infection and Immunity, April 1992, Vol. 60, No. 4, pages 1447-1454. See the entire document.	8-12
X	HOUSTON ET AL, Response of Guinea Pigs to a Vaccine Containing a New Adjuvant (SAF) and Gram-Negative Bacteria, Laboratory Animal Science, February 1995, Vol. 45, No. 1, p. 58-66. See the entire document.	8-12
X	EVANS ET AL, Immunization with Porphyromonas (Bacteroides) gingivalis Fimbriae Protects Against Periodontal Destruction, Infection and Immunity, July 1992, Vol. 60, No. 7, pages 2926-2935. See the entire document.	8-12
X	PERSSON ET AL, Immunization Against Porphyromonas gingivalis Inhibits Progression of Experimental Periodontitis in Nonhuman Primates, Infection and Immunity, March 1994, Vol. 62, No. 3, pages 1026-1031. See the entire document.	8-12
X	FROLOV ET AL, In vivo Exposure to Porphyromonas gingivalis up-regulates Nitric Oxide but Suppresses Tumour Necrosis Factor-Production by Cultured Macrophages, Immunology, March 1998, Vol. 93, No. 3, pages 323-328. See the entire document.	8-12
X	ZUBERY ET AL, Bone Resorption Caused by Three Periodontal Pathogens In Vivo in Mice Is Mediated in Part by Prostaglandin, Infection and Immunity, September 1998, Vol. 66, No. 9, pages 4158-4162. See the entire document.	8-12